



CORRELATION OF SERUM PROCALCITONIN LEVELS WITH WAGNER'S GRADING OF DIABETIC FOOT ULCER IN ACUTE DIABETIC FOOT INFECTIONS- A PROSPECTIVE STUDY

General Surgery

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ABSTRACT

Background: India is considered to be Diabetic capital of the world with estimated amount of 57.2 million people getting affected with type 2 diabetes mellitus by 2025. Complications of diabetes mellitus like ulcerations and subsequent bacterial infections are leading cause of lower extremity amputations. Early diagnosis and timely management of such complications is necessary to avoid dreadful life threatening incidents. Recent studies have shown that usage of biochemical pro inflammatory markers like procalcitonin are reliable source for early diagnosis of bacterial infections. A cross sectional study performed involving 94 infected diabetic foot patients, with diabetic history of more than one year. Serum procalcitonin levels were estimated at the time of presentation were undetectable in patients with grade 1 diabetic foot ulcers and raised levels of serum procalcitonin were found in higher grades of diabetic foot ulcer. It has been found out that raised levels of serum procalcitonin were found in higher grades of diabetic foot ulcer in case of acute diabetic foot infections. A final limitation is that we did not assess the time consumption and cost effectiveness of biochemical analysis of serum procalcitonin.

KEYWORDS

Procalcitonin, acute diabetic foot infections, foot and ankle surgeries

Introduction

Diabetes mellitus type 2 is considered to be one of the most widely spread disease around the globe which has been estimated to affect around 57.2 million people in India by 2025 according to World Health Organization (WHO) global estimate for prevalence of diabetes in 1993. Diabetic foot complications are notorious for their silent spread and sometimes left undiagnosed. Diabetic foot infections are one of the most life threatening complications of diabetes. About 2-3% of diabetic population are getting hospitalized due to diabetic foot ulcer every year. About 60% of non-traumatic lower extremity amputation are due to diabetic foot infections and its complications like osteomyelitis. As these complications potentially mask typical clinical features leads to hindering or delayed diagnosis. Hence use of traditional diagnosing methods like TLC are not enough in diagnosing or classifying acute diabetic foot infections. This lead to usage of acute phase reactants like Procalcitonin and CRP along with ESR as alternate diagnostic markers. All these markers can be used in diagnosing acute diabetic foot infection thereby avoiding its dreadful complications to some extent but reliability of such markers remains questionable.

Procalcitonin is a peptide precursor of calcitonin, composed of about 111 amino acids and is produced by Para follicular c-cells of thyroid gland and neuroendocrine cells of the lung and intestine. It is found when pre procalcitonin is cleaved by endopeptidase, the normal level of procalcitonin in the bloodstream is 0.01mcg/lit which is untraceable but its level starts raising in response to any proinflammatory stimulus especially seen in those that of bacterial origin, hence it is classed as an acute phase reactant. The induction period ranges from 4 to 12 hours and its half-life in the blood ranges from 22 to 35 hrs. [4] its level does not raise significantly in non-infectious inflammation or viral infections, the magnitude of the raise of serum procalcitonin levels has proven to correlate with the severity of the disease [5] but this high levels of procalcitonin produced during infections does not lead to subsequent increase in calcitonin or decrease in serum calcium levels.

Diabetic foot ulcers known to cause osteomyelitis of lower limb. Early diagnosis and prompt treatment of such devastating complications of diabetic foot ulcers is necessary to prevent major/minor amputation but there is no single laboratory marker which is both sensitive and

specific in diagnosing these infections with accuracy. Other acute phase reactants like ESR, CRP or TLC are not specific as they can be elevated in non-pyogenic pro inflammatory stimulus. Pus culture and sensitivity is not a true gold standard due to its varied positivity rates (40-70%). But serum procalcitonin at 0.5ng/ml is found to be an accurate marker of pyogenic bacterial pro-inflammatory stimulus.

The objective of this study is to show how raised procalcitonin levels related to severity of acute diabetic foot infection

Patients and methods

Study design

The present study is a cross sectional study involving 94 type 2 diabetic patients with diabetic foot infections, who met the inclusion criteria admitted in the time period of march 2019 to December 2019 in Vinayaka mission's medical college, Karaikal, Pondicherry, India.

Inclusion criteria

Type 2 diabetic patients admitted through diabetic foot clinic, department of general surgery in Vinayaka mission's medical college, Karaikal, Pondicherry, India between march 2019 to December 2019 were included in the study.

The presence of an ulcer with slough, pus, sinus, serous discharge from ulcer, necrotic tissue or signs of cellulitis was taken as clinical evidence of acute diay foot infection.

Exclusion criteria

1. Type 2 diabetes patient with Hansen's disease.
2. Type 2 diabetes patient with clinical evidence of vascular insufficiency.
3. Type 2 diabetes patient on immune-suppressants, multivitamins.
4. Patient with infections in sites excluding foot.
5. Wagner's grade 0 and 5 were excluded from the study.

Study procedure

A detailed clinical history, body mass index, history of smoking was recorded on proforma, clinical assessment including, peripheral pulse examination was done. All relevant laboratory investigation including serum procalcitonin levels, wound culture and sensitivity, radiograph

of affected part was done. Study population with diabetic foot infections were graded using Wagner's grading: Grade 0- intact skin; Grade 1- superficial ulcers of the skin or subcutaneous fascia; Grade 2- ulcers extending into the tendon, bone, or capsule; Grade 3- deep ulcers with osteomyelitis or abscess; Grade 4- gangrene of the toes or the forefoot; and Grade 5- gangrene of the mid foot or the hind-foot.

Estimation of procalcitonin

Diazyme's Procalcitonin (PCT) Assay is for the quantitative determination of PCT in Serum, EDTA or Lithium Heparin plasma samples. PCT should be measured according to specific application parameters for specific chemistry analyzers. Diazyme's PCT Assay kit consists of two liquid stable reagents; R1, and R2, and the PCT calibrators and controls are packaged separately. Diazyme's PCT methodology utilizes multiple monoclonal antibodies for enhanced assay sensitivity and specificity.

Diazyme's PCT Assay is based on a latex enhanced immunoturbidimetric method. PCT proteins in the sample bind to the specific anti-PCT antibody which is coated on latex particles, and causes agglutination. The degree of the turbidity caused by agglutination can be measured optically and is proportional to the amount of PCT in the sample. The chemistry analyzer calculates the PCT concentration of a sample by interpolation of the obtained signal of a calibration curve. The reaction is monitored at 600nm and completed within 10 minutes.

Treatment undergone

All the patients included in the study were admitted and started with empirical IV antibiotics after sending wound swab for culture. Glycemic control was achieved with appropriate insulin dosage. Thorough debridement, daily dressings and abscess drainage were performed. Patients were discharged with a healthy wound.

Outcome

The severity of the diabetic foot infections was graded using Wagner's grading, radiograph, debridement, and mortality were recorded. This data was compared with serum procalcitonin levels of respective patients.

Results

Total of 94 diabetic foot ulcer patients were eligible and taken into study, relevant consents obtained after ethical committee approval. There were no dropouts, no mortality in the study. Gender was not found to have influence on wound outcomes in the present study. Smokers and patients with co-morbidities like hypertension and CAD were excluded.

In the present study the mean age of the patient was 57.46 with standard deviation of 5.43. There were 66 male patients and 28 were female patients. Mean duration of diabetes mellitus was 8.24 years over all, in patients with grade 4 having the highest mean duration of diabetes mellitus was 10.12 years with least in patients with grade 1 ulcers of 7.9 years. Mean BMI of overall study population was 24.2 whereas in patients with grade 4 ulcers having highest BMI of 27.6 and least in grade 2 ulcers 23.8. At presentation patients with grade 1 ulcers had better glycemic control with mean FBS of 153mg/dl and with poor glycemic control in grade 4 ulcers with mean FBS of 256.4mg/dl. mean Total leucocyte count (TLC) of overall population was $16.4 \times 10^9/\text{lit}$, as the grade of ulcer increased TLC count increased in this study population. Procalcitonin levels in the study population had mean concentrations about 160.42pg/dl. (Table 1).

Table 1: Demographic and clinical data of the study

Demographic Data	
Age (years)	57.46±5.43
Gender (M/F)	66/28
Duration of DM(years)	8.24±6.62
BMI(kg/mt ²)	24.2±6.72
FBS(mg/dl)	162.6±67.83
HbA1C(%)	8.3±1.02
TLC (109/Lit)	16.4±4.45
Procalcitonin(Pg/dl)	160.42±92.68
Data are expressed as mean ± SD, BMI= Body Mass Index, FBS=Fasting Blood Sugar, HbA1c=Glycosylated hemoglobin, TLC= Total Leucocyte count.	

population.

In present study all participants were graded according to Wagner's grading. (Table 2) Grade 2 having the highest number of patients (35.1%), followed by grade 3 (31.9%), grade 1 (20.21%) and grade 4 having least patients (14.89%).

Table 2: Wagner's grading and number of patients.

WAGNER'S GRADING	NO. OF PATIENTS
GRADE 1	20 (20.21%)
GRADE 2	33 (35.1%)
GRADE 3	30 (31.9%)
GRADE 4	14 (14.89%)

Graph 1: Wagner's grading and number of patients.

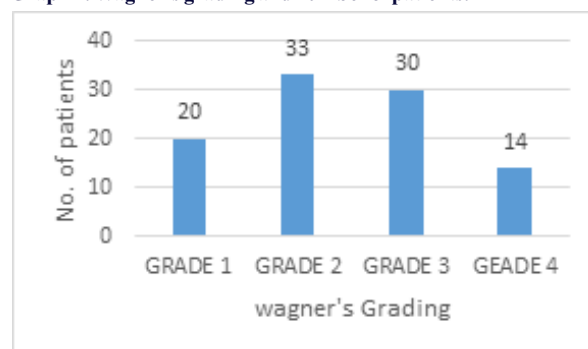
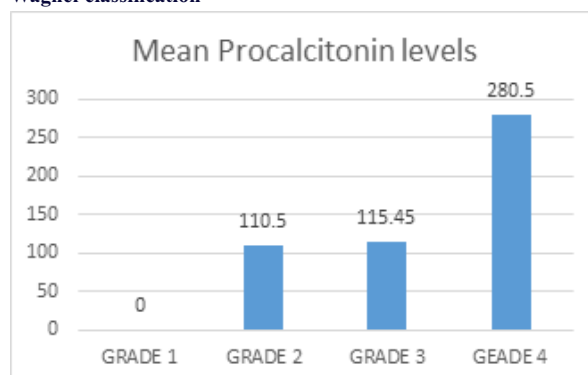


Table 3: Mean ± standard deviation of procalcitonin values among different types of diabetic foot infections according to Wagner classification

WAGNER'S GRADING	MEAN PROCALCITONIN LEVELS(pg/dl)
GRADE 1	UNDETECTABLE
GRADE 2	110.5±30.4
GRADE 3	115.45±38.6
GRADE 4	280.50±100.02

Graph 2: Mean ± standard deviation of procalcitonin values among different types of diabetic foot infections according to Wagner classification



Increase in grade of diabetic foot infections showed increase in procalcitonin levels as shown in the Table 3, significant increase in procalcitonin was found in grade 4 ulcers with mean value of 280.50ng/dl which was significant.

Discussion

Diabetic foot infection is one of the most common complications of diabetes mellitus and the most common cause for major and minor amputations, which need early detection and prompt treatment with antimicrobials and glycemic control.

This study aims in Correlation of a proinflammatory marker-procalcitonin levels with grade of diabetic foot ulcer to determine the severity of bacterial infection. Some of the previous studies have shown that procalcitonin can be a reliable marker for bacterial infection whereas the other studies did not support the observation. We hereby aimed to evaluate the sensitivity of serum procalcitonin in diagnosing bacterial infections and its raised serum levels with the severity of infections.

Increased serum procalcitonin levels were seen in minor systemic

bacterial infections as a part of inflammatory response as well as in severe sepsis or septic shock as a part of systemic inflammatory response syndrome. However, levels of serum procalcitonin in minor infections although raised but found out to be not raised as high as in case of severe sepsis or septic shock.

In this study we have found out that higher levels of procalcitonin consistent with more severe higher Wagner's diabetic foot ulcer grading in case of infected diabetic foot ulcer patients. So procalcitonin can be a reliable marker in diagnosis of bacterial infections, diagnosis of bone infections and differentiating gram negative sepsis from gram positive in diabetic foot ulcers.

The results of this study may not be consistent with the general diabetic population with absence of foot related complications. Final limitation of this study is that we could not establish time consumption and cost efficacy of evaluating serum procalcitonin levels. Our study is to evaluate the sensitivity of serum procalcitonin levels in diagnosing bacterial infections and correlating its raised levels with the severity of infections.

CONCLUSION

Serum procalcitonin is still not considered as an important tool in diagnosing bacterial infections. Surgeons should be aware of increased risk of diabetic foot complications resulting from the delay in diagnosis and management of diabetic foot infections, risk of minor and major amputations, sepsis and septic shock. Surgeons should consider measuring serum procalcitonin levels not only in all suspected diabetic foot ulcer patients but also in any suspected bacterial infections.

Although foot and ankle surgeons are largely concerned with diabetic foot infections and its complications, evaluation of serum procalcitonin can help in prevention of sepsis and septic shock along with requirement of major and minor amputation. Hence procalcitonin can be used as an early and reliable marker in diagnosis of bacterial infections.

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